

### Remarks

The March 31, 2004 Official Action has been carefully reviewed. In view of the amendments submitted herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset it is noted that a shortened statutory response period of three (3) months was set in the March 31, 2004 Official Action. Therefore, the initial due date for response is June 30, 2004. This amendment and request for reconsideration is being filed before expiration of the initial response period.

At page 3 of the Official Action, the Examiner contends that claims 1, 4, 6, 8-10, and 12 fail to satisfy one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. §120.

Claims 1, 4, 6, 8-10, and 12 are rejected for allegedly failing to satisfy the written description and enablement requirements under 35 U.S.C. §112, first paragraph.

Claims 1-12 stand rejected under 35 U.S.C. §102(a,b) as allegedly anticipated by Severinov et al. (J. Biol. Chem. (1998) 273:16205-16209).

The foregoing rejections constitute all of the grounds set forth in the March 31, 2004 Official Action for refusing the present application.

Claims 2 and 12 have been cancelled by this amendment. Claim 1 has been amended to recite the limitations previously set forth in claim 2. No new matter has been introduced into this application by reason of any of the amendments presented herewith.

The grounds of rejection set forth in the March 31, 2004 Official Action, which are summarized above, are inapplicable to the claims as presently amended. Those grounds of rejection are, therefore, respectfully traversed for the reasons set forth hereinbelow.

THE INSTANTLY CLAIMED SUBJECT MATTER IS SUFFICIENTLY DISCLOSED  
IN U.S. PATENT APPLICATION 09/191,890 AND U.S. PROVISIONAL  
APPLICATION 60/065,391 TO WARRANT THE BENEFIT OF THE EARLIER  
FILING DATE UNDER 35 U.S.C. §120

It is the Examiner's position that Applicants are not entitled to the benefit of an earlier filing date under 35 U.S.C. §§119(e) or 120 because the term "conjugated thiol" is not described in the parent application or the original provisional application in such a manner as to satisfy the requirements of 35 U.S.C. §112, first paragraph. The Examiner also contends that 1) the term "alkyl ester" in claim 12 is not supported in the parent or provisional application and 2) that there is new matter in the instant specification at page 22, line 6 and the bottom of page 28 to the top of page 29. Thus, the Examiner asserts that the instant application is a continuation-in-part of U.S. Application 09/191,890 and sets the filing date of the instant application (July 12, 2001) as the priority date for purposes of prior art.

At the outset, Applicants vigorously dispute the Examiner's contention that the instant application is a continuation-in-part of U.S. Patent Application 09/191,890. Applicants respectfully submit that the specifications of the two applications are essentially identical. Indeed, Applicants respectfully point out to the Examiner that U.S. Patent Application 09/191,890 plainly recites the phrase "ethanethiol is a preferred reactant" at page 22, line 6, as in the instant application. Additionally, Applicants submit that the specification of U.S. Patent Application 09/191,890 from page 28, line 28 through page 29, line 10 is identical to the passage at page 28, line 28 through page 29, line 10 of the instant application. Thus, Applicants respectfully submit that there is no new matter added in the instant application as compared to U.S. Patent Application 09/191,890. Accordingly, the instant application is a **continuation** of U.S. Patent Application 09/191,890, as declared on the transmittal sheet for the instant application.

Additionally, Applicants strenuously disagree with the Examiner's position that the term "alkyl ester" in claim 12 is not supported by the parent or provisional applications. Applicants respectfully submit that claim 12 does not recite the term "alkyl ester." Indeed, claim 12 refers to an "alkyl thiol." Support for an "alkyl thiol" and the subject matter claimed in claim 12 can be found throughout both the instant specification and the specification of U.S. Patent Application 09/191,890. For example, at page 14, lines 17-19 of both specifications, the reaction solution is taught to also comprise an alkyl thiol. However, in an effort to expedite prosecution of the instant application, Applicants have cancelled claim 12 thereby rendering moot the Examiner's contention that the subject matter claimed in claim 12 contains new matter.

As noted herein, Applicants have amended claim 1 to recite that the "conjugated thiol" is selected from the group consisting of thiophenol, 1-thio-2-nitrophenol, 2-thiobenzoic acid, 2-thiopyridine, 4 thio-2-pyridine carboxylic acid and 4-thio-2-nitropyridine. This group of conjugated thiols is explicitly recited in both the parent application and the original provisional application. Indeed, claim 4 of the parent application recites the same group of conjugated thiophenols that is now recited in claim 1 of the present application. Furthermore, parent U.S. Patent Application 09/191,890 discloses at page 22, lines 3-7, as in the instant application, that thiophenol may be employed in the methods of the invention as well as "conjugated thiols such as 1-thio-2-nitrophenol, 2-thiobenzoic acid, 2-thiopyridine, ethanethiol is a preferred reactant. 4 thio-2-pyridine carboxylic acid and 4-thio-2-nitropyridine." A similar disclosure also appears at page 7, lines 12-16 and claim 2 of U.S. Provisional Application 60/065,391, with the omission of the phrase "ethanethiol is a preferred reactant." It is also noteworthy in this regard that claims 3-11 of the instant application are

identical to claims 3-11 of U.S. Provisional Application 60/065,391. Thus, Applicants respectfully submit that the disclosure of the above-identified group of compounds is described in the parent and provisional applications in such a manner as to satisfy all of the requirements of 35 U.S.C. §112, first paragraph.

In view of all of the foregoing, Applicants respectfully submit that the instantly claimed subject matter is plainly entitled to a priority date of November 13, 1997, the filing date of U.S. Provisional Application 60/065,391.

**CLAIMS 1, 4, 6, 8-10 AND 12 SATISFY THE WRITTEN DESCRIPTION  
AND ENABLEMENT REQUIREMENTS UNDER 35 U.S.C. §112, FIRST  
PARAGRAPH**

The Examiner has rejected claims 1, 4, 6, 8-10, and 12 for allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph. Specifically, it is the Examiner's position that the term "conjugated thiol" reads on conjugated alkyl and aryl compounds. The Examiner contends that the specification fails to describe conjugated alkyl compounds capable of efficiently catalyzing both the cleavage and ligation steps of the instantly claimed method. The Examiner further asserts in this regard that the specification is not enabling for conjugated alkyl compounds because the specification fails to provide a "critical core structure" of the compounds.

Applicants respectfully disagree with the Examiner. The Examiner has relied on the passage at page 22, lines 3-7 which reads, in part, "other equivalents [of thiophenol] are conjugated thiols such as 1-thio-2-nitrophenol, 2-thiobenzoic acid, 2-thiopyridine, ethanethiol is a preferred reactant. 4 thio-2-pyridine carboxylic acid and 4-thio-2-nitropyridine." Applicants submit that the phrase "ethanethiol is a preferred reactant." is clearly a word processing error. From a purely grammatical viewpoint, the statement "ethanethiol is a

preferred reactant." is inconsistent with the other members of the compound grouping in that it is a complete sentence and not a simple recitation of a compound name. Indeed, the above-mentioned statement introduces a stray period into the middle of the sentence that encompasses it. Furthermore, as noted by the Examiner, ethanethiol is not conjugated, i.e. possessing alternating single and double bonds. Inasmuch as the inclusion of a thiol containing compound which is not conjugated in a list of "conjugated thiols" would be repugnant to the plain meaning of "conjugated thiol," Applicants submit that a skilled artisan would conclude that the phrase "ethanethiol is a preferred reactant." was inadvertently inserted into the list of compounds, especially in view of the fact that ethanethiol is not a conjugated thiol. Indeed, at page 14, lines 18-19, ethanethiol is identified as an alkyl thiol. As noted by the Examiner in the instant Official Action, alkyl thiols may be employed **in addition** to conjugated thiols. Furthermore, certain alkyl thiols are demonstrated in the specification to be unable to catalyze both cleavage and ligation by themselves, as required by claim 1 (see, for example, page 24, lines 5-18). Thus, the term "conjugated thiol" does not read on unconjugated alkyl compounds such as ethanethiol.

It is noteworthy in this connection that U.S. Provisional Application 60/065,391, incorporated by reference into the instant application, clearly identifies conjugated thiols as "1-thio-2-nitrophenol, 2-thiobenzoic acid, 2-thiopyridine, 4 thio-2-pyridine carboxylic acid and 4-thio-2-nitropyridine" (page 7, lines 14-16) as useful conjugated thiols, in addition to thiophenol, per se. Notably, this list is the same as the one provided at page 22, lines 5-7 of the instant application, with the exception of the clearly misplaced statement "ethanethiol is a preferred reactant."

In the interest of expediting prosecution of the instant application, Applicants have amended claim 1 to

include the subject matter set forth in claim 2, so that claim 1 now specifies that the conjugated thiol is selected from the group consisting of thiophenol, 1-thio-2-nitrophenol, 2-thiobenzoic acid, 2-thiopyridine, 4 thio-2-pyridine carboxylic acid and 4-thio-2-nitropyridine. Inasmuch as the conjugated thiols are now explicitly defined in claim 1, Applicants submit that the rejection of claims 1, 4, 6, 8-10, and 12 for allegedly failing to satisfy the written description requirement under 35 U.S.C. §112, first paragraph is untenable and respectfully request its withdrawal.

**CLAIMS 1-12 ARE NOT ANTICIPATED BY SEVERINOV ET AL.**

Claims 1-12 stand rejected under U.S.C. §102(a,b) as allegedly anticipated by Severinov et al. (J. Bio. Chem. (1998) 273:16205-16209). Specifically, the Examiner cites Severinov et al. for its disclosure of a method for the ligation of an expressed protein comprising an intein-chitin binding domain with a peptide containing an unoxidized sulfhydryl side chain in the presence thiophenol in a "single-pot" reaction.

The Examiner has accorded only the filing date of the instant application (July 12, 2001) for claims 1-12, thereby allowing Severinov et al. to be cited as prior art. As established hereinabove, however, the claimed invention should rightfully be accorded the priority date of the filing of U.S. Provisional Application 60/065,391 (November 13, 1997). By contrast, Severinov et al. was published on June 26, 1998, which is after the priority date (November 13, 1997) of the instant application. Accordingly, Severinov et al. can not be properly cited as prior art against claims 1-12 as now amended.

In light of the foregoing, Applicants respectfully submit the rejection of claims 1-12 under 35 U.S.C. §102(a,b) is untenable and request its withdrawal.

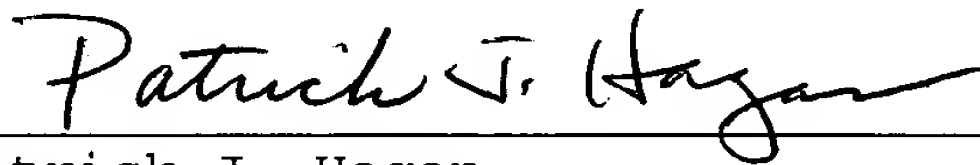
### CONCLUSION

In view of the amendments presented herewith, and the foregoing remarks, it is respectfully urged that the rejections set forth in the March 31, 2004 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number give below.

Respectfully submitted,  
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